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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/804,176

03/12/2001

Sean Ekins

PC10697A

1034

7590

05/20/2005

EXAMINER

BRUSCA, JOHN S

Paul H. Ginsburg

Pfizer Inc

235 East 42nd Street, 20th Floor

New York, NY 10017-5755

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 05/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/804,176

Applicant(s)

EKINS, SEAN

Examiner

John S. Brusca

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 February 2005.
- 2a) ☐ This action is **FINAL**.      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 3,16-22,24-33,41 and 42 is/are pending in the application.
- 4a) Of the above claim(s) 16-22,24,27-33,41 and 42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13 and 26 is/are rejected.
- 7) ☐ Claim(s) 25 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: See Continuation Sheet.

Continuation of Attachment(s) 6). Other: email from Accelrys of 5/5/2005.

### **DETAILED ACTION**

1. This Office action is a non-final Office action in view of the new grounds of rejection regarding prior art for CATALYST Version 4 not necessitated by the applicant's amendment.
2. Claim 25 is improperly listed as withdrawn. Presumably the applicants listed claim 25 as withdrawn in view of the amendment filed 15 February 2005 which makes claim 25 depend from cancelled claim 23. However the status of claim 25 should be indicated as original in future claim listings. Claim 25 was examined in the Office action mailed 07 December 2004.
3. The applicants have pointed to an inconsistency in the status of claim 26 in the Office action mailed 07 December 2004. Claim 26 was rejected under 35 U.S.C. § 101 and indicated as rejected on the Office action summary, but was indicated as containing allowable subject matter and objected to for depending from a rejected claim. Claim 26 was incorrectly indicated as containing allowable subject matter in the Office action mailed 07 December 2004. The Office regrets any inconvenience this error may have caused the applicants.
4. An associate power of attorney was filed 15 February 2005, however the Office abolished the associate power of attorney practice on 25 June 2004 when 37 CFR 1.34 was eliminated (see 69 Fed. reg. 29865 (May 26, 2004) and 1283 Off. Gaz. Pat. Office 148 (June 22, 2004)). The associate power of attorney will not be recognized by the Office.

### ***Specification***

5. The objection to the abstract in the Office action mailed 07 December 2004 is withdrawn in view of the amendment filed 15 February 2005.

***Claim Objections***

6. The objection to claims 14, 15, and 38 in the Office action mailed 07 December 2004 is withdrawn in view of the cancellation of the claims in the amendment filed 15 February 2005.
7. Claim 25 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 25 is improper because it depends from cancelled claim 23.

***Claim Rejections - 35 USC § 101***

8. The rejection of claims 23, 25, and 39 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter in the Office action mailed 07 December 2004 is withdrawn in view of the cancellation of claims 23 and 39 (which causes claim 25 to be an improper dependent claim) in the amendment filed 15 February 2005.

9. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claim 26 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is drawn to data or data that is entirely non-functional descriptive material on computer readable media. See MPEP 2106.

***Claim Rejections - 35 USC § 112***

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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12. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 contains the trademark/trade name CATALYST. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a computer program and, accordingly, the identification/description is indefinite.

***Claim Rejections - 35 USC § 102***

13. The rejection of claims 1, 2, 4-6, 10, 11, 13-15, 23, 25, 39, 40, and 43 are rejected under 35 U.S.C. 102(a) as being anticipated by Ekins et al. in the Office action mailed 07 December 2004 is withdrawn in view of the cancellation of claims 1, 2, 4-6, 10, 11, 13-15, 23, 39, 40, and 43 in the amendment filed 15 February 2005.

***Claim Rejections - 35 USC § 103***

14. The rejection of claims 1, 7-9, and 38 under 35 U.S.C. 103(a) as being unpatentable over Ekins et al. in the Office action mailed 07 December 2004 is withdrawn in view of the cancellation of claims 1, 7-9, and 38 in the amendment filed 15 February 2005.

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15. The rejection of claims 1 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ekins et al. in view of Wu et al. in the Office action mailed 07 December 2004 is withdrawn in view of the cancellation of claims 1 and 12 in the amendment filed 15 February 2005.

16. The rejection of claims 34-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ekins et al. in view of Rogers et al. in the Office action mailed 07 December 2004 is withdrawn in view of the cancellation of claims 34-37 in the amendment filed 15 February 2005.

17. The rejection of claims 1, 2, 4-11, 13-15, 23, 25, 38, 39, 40, and 43 under 35 U.S.C. 103(a) as being unpatentable over Strobl et al. in view of Lane in view of Hopfinger et al. in the Office action mailed 07 December 2004 is withdrawn in view of the cancellation of claims 1, 2, 4-11, 13-15, 23, 38, 39, 40, and 43 in the amendment filed 15 February 2005.

18. The rejection of claims 1 and 12 under 35 U.S.C. 103(a) as being unpatentable over Strobl et al. in view of Lane in view of Hopfinger et al. and further in view of Wu et al. in the Office action mailed 07 December 2004 is withdrawn in view of the cancellation of claims 1 and 12 in the amendment filed 15 February 2005.

19. The rejection of claims 34-37 under 35 U.S.C. 103(a) as being unpatentable over Strobl et al. in view of Lane in view of Hopfinger et al. and further in view of Rogers et al. in the Office action mailed 07 December 2004 is withdrawn in view of the cancellation of claims 34-37 in the amendment filed 15 February 2005.

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

21. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

22. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ekins et al. in view of the admission of prior art of CATALYST version 4 in the instant specification.

The claims are drawn to a method of making a pharmacophore of an inhibitor of cytochrome protein CYP2D6. The training set of inhibitors includes 5 or more selective serotonin reuptake inhibitors (SSRI). Multiple conformations of each training set molecule is considered and one or more pharmacophores are generated with multiple chemical property features. The steps of the method are executed by a computer program named CATALYST version 4.

Ekins et al. shows in the abstract and throughout a method of making a pharmacophore of inhibitors of CYP2D6. Table 1 shows some members of a training set that includes multiple SSRI compounds with  $K_i$  values ranging from 0.03 to 529.51. On page 479 Ekins et al. details a computer mediated method of making a pharmacophore in which multiple conformations of each inhibitor are considered. Ekins et al. shows conformers with an energy range of 20 Kcal/mole were used. Ekins et al. does not show an energy range of conformers of either 10, 35, or 50 Kcal/mole. Ekins et al. states on page 478 that CYP2D6 is involved in the metabolism of many



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drugs and that it is desirable that new drugs not inhibit the activity of CYP2D6. Ekins et al. shows on page 479 that the steps of the method are executed by a computer program named CATALYST version 2.3 or 3.1. Ekins et al. does not show use of CATALYST version 4.

The specification provides an admission of prior art by another on page 42, lines 4-5, which shows that the applicant purchased CATALYST version 4 from Molecular Simulation. The availability of a subsequently released version of the program, CATALYST version 4.5, in 1999 is shown by the attached email dated 05 May 2005 from Accelrys (the successor to the firm Molecular Simulation).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Ekins et al. by use of the computer program CATALYST version 4 because the later version 4 was publicly available prior to the effective filing date of the instant application (14 March 2000), as shown by the use of version 4 by the applicant in the instant specification and by the showing of Accelrys. The description of CATALYST version 4 as being available from Molecular Simulation in the instant specification constitutes an admission of the applicant of the work of another as prior art (see MPEP 2129).

### ***Conclusion***

23. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of

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the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

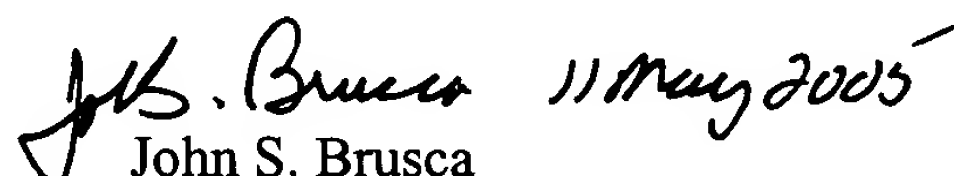
For all other customer support, please call the USPTO Call Center at (800) 786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, PhD. can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

 11 May 2005  
John S. Brusca  
Primary Examiner  
Art Unit 1631

jsb

**Brusca, John**

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**From:** Shannon Huang [huang@accelrys.com]  
**Sent:** Thursday, May 05, 2005 11:08 AM  
**To:** Brusca, John  
**Subject:** Catalyst release?

---

Dear John:

Please see the attachment and let me know if you need any additional information.

Thanks.

Shannon  
Shannon Huang  
Senior Contract Specialist  
Accelrys Software Inc.  
10188 Telesis Court, Suite 100  
San Diego, CA 92121-4779  
(858)799-5402  
(858)799-5100 Fax

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----- Forwarded by Shannon Huang/San Diego/Accelrys on 04/27/2005 08:04 AM -----

Samuel Toba/San Diego/Accelrys

To: Shannon Huang/San Diego/Accelrys@Accelrys  
cc

04/26/2005 05:22 PM

Subject: Re: Catalyst 4.0 release? [Link](#)

I do not have the historical Catalyst from first release, but I have the approx time line release since 1999 along with what's new in them.

I have attached the document for your information.

Pls let me know if I can help further.

Many thanks,  
-Samuel

5/5/2005



## Enhancements to CATALYST (1999 - present)

### *Catalyst 4.5 Release 1999*

- **Variable Weighting/Variable Tolerance:** HypoGen was enhanced to permit optimization of the weights and tolerances associated to each feature in a pharmacophore model to vary in relative importance. When turned on, the generated HypoGen models contain features that differ in weighting (magnitude of contribution to activity), or tolerance (magnitude of location constrain)

### *Catalyst 4.6 Release 2000*

- **Partial Match Searching:** Automation of 'leave-one-out' permutation of pharmacophore model in searching. Improved database searching efficiency.

### *Catalyst 4.7 Release 2002*

- **Conformation Generation Feature:** The catDBLibrary module features a novel means of building Catalyst-formatted databases of very large virtual (and real) combinatorial libraries from Markush template.
- **New Platform Support:** All Catalyst applications were optimized to run on two additional server platforms - Linux and AIX. Oracle support is provided for both Linux and IRIX. The availability of these platform provides enhanced speed-up in pharmacophore model generation, database building and 3D searching.
- **MultiBlob Scaling:** This enhancement is a user-tuneable parameter that completely eliminates negative fit scores. This change can be assessed in the Catalyst file input setting.
- **Feature Mapping:** Pharmacophore listing output to include projected point coordinates, and hence directionality in ligand-receptor interaction.

### *Catalyst 4.8 Release June 2003*

- **Iterative Algorithm Enhancement:** The Ferro-Hermans iterative algorithm for fitting was replaced with the Kabsch analytical algorithm. The latter algorithm gives an exact solution rather than an approximation. This leads to higher accuracy in computed fit scores and alignments.
- **More than 10 Hypos Reported by HypoGen:** User can now request that HypoGen export more than 10 hypotheses overriding the default setting of 10 (previously fixed).

- **Conformer Generation:** Improvement to cis/trans ratio distribution in peptide bonds and *equatorial/axial* distributions in 1,4 disubstituted piperidine rings for BEST conformer generation and analysis.
- **Automated Identification of Excluded Volumes:** HypoRefine is a new Catalyst module that permits simulated annealing optimization of excluded volumes in activity-based hypothesis generation. This module adds one or more excluded volumes to HypoGen models, improving regression scores and accuracy of model predictions. For systems where steric effect plays a role in modulating biological activity, HypoRefine provides more realistic pharmacophore-based SAR model for activity trends between several ligands and a receptor target.

### ***Catalyst 4.9 Release December 2003***

- **Linux Client + Server:** The release of Catalyst 4.9 provides a client port to Linux Red Hat WS2.1 making Catalyst an integrated one-box solution on Linux.

### ***Catalyst 4.9.1 Release March 2004***

- **Linux Client + Server:** The release of Catalyst 4.9.1 provides an expanded Linux client and server port to Linux Red Hat Enterprise WS2.1, WS3.0 and Red Hat 9. Catalyst also continues to provide support for multiple Server platforms - Linux, IRIX, and AIX.

### ***Catalyst 4.10 Release January 2005***

- **Excluded Volume in HipHop:** Excluded Volume (HypoRefine) tool for model refinement currently available in HypoGen will be added to the HipHop algorithm. This would enable use of 'negative' (non-binding) ligand information to enrich pharmacophore model quality.
- **Alignment tool enhancements:** Provide a mechanism/option for exporting ligands aligned to a query (without shifting the coordinates of the queries) and exporting queries aligned to the ligand without shifting the coordinates of the ligand. Ideal in combining Catalyst info with known target-ligand structural info.
- **Automated statistical estimate of model quality:** Allow user to utilize Fischer Randomization approach to evaluate the statistical significance/quality of Catalyst generated hypothesis model.
- **Use of 3<sup>rd</sup> party conformers without recalculating energy:** User can import conformers and energies generated outside Catalyst for use in pharmacophore model generation and database search.
- **New torsional parameter for sulfonamides:** A new torsional parameter (X-S-N-X) has been included to favor torsions observed from ligand complexes from crystal structures.
- **Double precision and new algorithm implementation:** Algorithm changes and modifications to enable the use of double precision allow Catalyst to have platform independent (no differences greater than 1e-5). This is useful for users to take advantage of Catalyst multiple platforms support of IRIX, Linux, and AIX.